Remarks

Rejection of Claims 1-17 and 19-37 Under 35 U.S.C. 103(a)

Claims 1-17 and 19-37 stand rejected under 35 U.S.C. 103(a) as allegedly obvious over EP 0 521 562 in view of EP 0 678 295, EP 0 159 237, GB 2002319, and JP05194253. The applicants maintain their previous arguments regarding the cited art and traverse the Office Actions' assertions regarding the teachings of the cited art. Based upon these arguments alone, the claims are non-obvious in view of the cited art.

The pending claims are drawn to powders of reversed vesicles and processes of making the powders. The powders of reversed vesicles comprise one or more non-ionic surfactants, whereby when the powder is dispersed in a biodegradable oil the percent yield of reversed vesicles is greater than when the same amount of reversed vesicles is prepared directly in the biodegradable oil. In their previous responses the applicants argued that the property recited in the whereby clause was unexpected and, therefore, rendered the presently claimed compositions and methods non-obvious over the cited art.

The Office asserts that the prior art does not suggest the use of biodegradable oil in the preparation of vesicles and that EP 562 teaches the use of "synthetic oil just as in the instant application." The applicants do not understand the relevance of these assertions and believe the Examiner may have misunderstood their position. The applicant's position has nothing to do with how the compositions are made. Rather, it is that the presently claimed compositions possess a property that is unexpected, rendering the claims nonobvious. *In re Papesch*, 315 F.2d 381, 137 USPQ 43 (CCPA 1963). There is nothing in the prior art that teaches or suggests that even if one were to modify the prior art compositions to arrive at the instantly claimed compositions that such compositions would have this property.

In commenting on the applicants' similar comments in previous responses, the examiner stated on page 3 of the present final office action:

> applicant misunderstood the Examiner's position. The examiner who did not question the presumed unexpected nature of the results the examiner was pointing that EP 562 does not teach the use of oil during the preparation of the vesicles and therefore, one would expect the same nature of results is obtained by applicant when subject to further treatment whether those results are unexpected or not.

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Although it is not entirely clear to the applicants, the examiner appears to be alleging that it would have been obvious to modify the compositions of EP 562 to arrive at the instantly claimed compositions, and, further, one would expect such compositions to have the property that applicant is asserting is unexpected. The applicants respectfully submit that the examiner has provided no basis for this assertion. Where in the prior art is there a teaching or suggestion that a powder of reversed vesicles as presently claimed would yield more reversed vesicles when dispersed in a biodegradable oil compared to the same amount of reversed vesicles directly made in the biodegradable oil? The applicant respectfully submits that there is no such teaching or suggestion. Accordingly the rejection cannot stand.

The present final office action alleges that it would have been obvious from the secondary references EP 0 678 295, EP 0159237, GB 2002319, and JP 05194253 to modify the dispersion of EP 562 to arrive at the presently claimed compositions. In addition to the argument above (which, in itself, should establish the nonobviousness of the present claims), the cited art fails to render the present claims obvious for the following reasons.

The vesicular preparation of EP 562 is a **dispersion** whereas the instant claims are directed to a **powder**. The dispersions of EP 562 have a nonpolar dispersion vehicle (which is lacking in the presently claimed powders) and none of the references, alone or in combination, suggest removing it, nor do they enable a method for removing the nonpolar excipient(s). Thus, not only is there no suggestion to combine the references as the examiner has done, combining them would not yield the presently claimed compounds and methods.

EP 0 678 295 is concerned with the problem of incorporating an active agent into liposomes, which are surfactant-based (phospholipid) bilayer systems formed in aqueous (polar) solutions (column 1, line 13-19), with the aim of providing liposomes with a high active agent encapsulating efficiency (column 1 line 3-6 and line 50-54). One of ordinary skill in the art would not, however, turn to EP 0 678 295 for teachings to modify the compositions of EP 562 to arrive at the instantly claimed compositions because these teachings are not concerned with removing non-polar excipients from a vesicular system. To the contrary, EP 0 678 295 discloses the removal of:

> a non-polar solvent from a solution of active agent/phospholipid (surfactant) and optionally a polar solvent (ethanol, water or mixtures thereof) from a vesicular system

Furthermore, EP 0 678 295 only seeks to increase the amount of drug incorporated in the liposomes and not the yield of liposomes in the aqueous solution.

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EP 0 159 237 is concerned with the problem of preparing solid (page 1 line 3) unit-dose forms of an oil-in-water emulsion for oral administration (page 1, line 2-6), that overcome the disadvantages of liquid emulsions, while retaining their advantages (page 2, line 25 - page 3, line 1-2): both physically and chemically stable over an increased period of time and an easy way of orally administering a fixed dose of a liquid emulsion. EP 237 mentions on page 6, line 16-22, that in the prior art methods of preparation of pharmaceutical, dietetic, or cosmetic forms by lyophilization of at least one active ingredient in solution or suspension in water or an organic solvent or else in an emulsion of the oil-in-water type had been proposed. It teaches a solution whereby an oil-in-water emulsion is prepared according to conventional methods, thereafter distributed over unit-dose alveolar packs and subsequently freeze-dried (page 6, line 23 - page 8, line 10). EP 237 does not teach or suggest modifying the compositions of EP 562 to arrive at the instantly claimed compositions because the teachings of EP 237 are not concerned with removing non-polar excipients from a vesicular system.

GB-2 002 319 is concerned with the problem of conservation of liposomes, which are in the form of a colloidal dispersion in an aqueous medium (page 1, line 5-6), in order to improve shelf-life (page 1, line 20) (see also page 1, line 23-25). For this purpose GB-2 002 319 teaches a process for the dehydration of a liposome colloidal dispersion in an aqueous liquid medium, which comprises (see page 1, line 26-30):

> mixing a hydrophilic compound (which is a must according to page 1, line 39-45 to avoid a sticky, oily residue, which is not suitable to provide after reconstitution with water a homogeneous colloidal liposomes dispersion in water) with
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> the liposome dispersion and
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> subjecting the obtained mixture to a dehydration process, preferably by freeze-drying (page 1, line 31-34) and
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> obtaining a stable powder.

Again, GB 319 does not teach or suggest modifying the compositions of EP 562 to arrive at the instantly claimed compositions because the teachings of GB 319 are not concerned with removing non-polar excipients from a vesicular system. To the contrary (and similarly to EP 0 678 295), GB 319 discloses the removal of a polar vehicle (water) from a vesicular system.

Furthermore, on page 2 in Table I it was even disclosed that the process for removing the dispersion vehicle leads to a reduction of 30% in the yield of undamaged liposomes and not to an increase, as has been observed by the inventors of the present application on removing the non-polar dispersion vehicle and subsequently re-dispersing the powder in a biodegradable oil (see examples 3 - 5).

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JP-05-194253 is concerned with the preparation of sustained-release microcapsules consisting of a biodegradable polymer loaded with water soluble polypeptide hormones by means of first preparing a reversed micelles solution thereof, precipitating the components with ethanol, re-dissolving the precipitate in another apolar vehicle, adding the polymers to the solution, subsequently adding water to form an emulsion, and thereafter removing all solvents.

As previously explained, reversed micelles are not at all stable systems, cannot be retrieved,and are therefore irrelevant to the presently claimed subject matter. Therefore, one of ordinary skill in the art would not use the teachings of this publication.

Lastly, each of the references cited addresses issues not directly related to the instantly claimed compositions and, therefore, they do not suggest combination as in the present rejection. One of ordinary skill in the article, given the divergent teachings, would not combine the art and the examiner has done to arrive at the presently claimed compositions and methods. Rather, they applicants respectfully submit that the examiner has selectively extracted teachings from the references to arrive at the presently claimed invention without any suggestion or motivation in the references themselves to do so.

For all of the foregoing reasons, the applicants respectfully request reconsideration and withdrawal of this § 103 rejection.

If the Examiner believes that a telephone or personal interview would expedite prosecution of the instant application, the Examiner is invited to call the undersigned attorney at (312) 913-2135.

Respectfully submitted,

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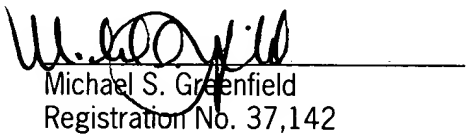

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